

**This Page Is Inserted by IFW Operations  
and is not a part of the Official Record**

## **BEST AVAILABLE IMAGES**

**Defective images within this document are accurate representations of the original documents submitted by the applicant.**

**Defects in the images may include (but are not limited to):**

- **BLACK BORDERS**
- **TEXT CUT OFF AT TOP, BOTTOM OR SIDES**
- **FADED TEXT**
- **ILLEGIBLE TEXT**
- **SKEWED/SLANTED IMAGES**
- **COLORED PHOTOS**
- **BLACK OR VERY BLACK AND WHITE DARK PHOTOS**
- **GRAY SCALE DOCUMENTS**

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

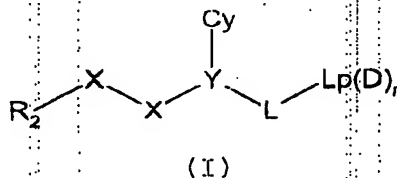
- 3 -

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1 (currently amended): A serine protease inhibitor of formula (I):



wherein:

R<sub>2</sub> is:

(i) phenyl optionally being substituted in the 3 and/or 4 position by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub>- or R<sub>1</sub>, and optionally substituted at the 6 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(ii) naphth-2-yl optionally substituted at the 6 or 7 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>; and optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by halo, haloalkoxy,

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 4 -

haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) pyrazol-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(ix) pyrid-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(x) pyrid-3-yl optionally substituted at the 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(xi) benzofur-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(xii) indol-2-yl optionally substituted on the indole nitrogen atom by alkyl and optionally substituted at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(xiii) indol-6-yl substituted at the 5 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio and optionally substituted at

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 5 -

the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>; or

(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;

R<sub>1</sub> is hydrogen; hydroxy; alkoxy; alkyl; alkylaminoalkyl; alkanoyl; hydroxyalkyl; alkoxyalkyl; alkoxycarbonyl; alkylaminocarbonyl; alkylamino; carboxyl; carboxymethyl; amido (CONH<sub>2</sub>) or amidomethyl;

R<sub>1j</sub> is: hydrogen; hydroxy; alkoxy; alkyl; alkanoyl; hydroxyalkyl; alkoxyalkyl; alkoxycarbonyl; alkylamino; carboxyl; carboxymethyl; amido (CONH<sub>2</sub>) or amidomethyl;

~~a 5 or 6 membered aromatic carbon ring optionally interrupted by a nitrogen, oxygen or sulphur ring atom, optionally being substituted in the 3 and/or 4 position (in relation to the point of attachment of X X) by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub> or R<sub>1</sub>, or the substituents at the 3 or 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>, and optionally substituted in the position alpha to the X X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio with the proviso that R<sub>2</sub> cannot be aminoisoquinolyl;~~

X-X is CONH;

~~each X independently is a C, N, O or S atom or a CO, CR<sub>1a</sub>, C(R<sub>1a</sub>)<sub>2</sub> or NR<sub>1a</sub> group, at least one X being C, CO, CR<sub>1a</sub>~~

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 6 -

~~or  $G(R_{1a})_2$ ;~~

~~each  $R_{1a}$  independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxyacetyl, alkylaminocarbonyl, alkoxyacetylaminomethyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;~~

~~$R_1$  is as defined for  $R_{1a}$ , provided that  $R_1$  is not unsubstituted aminoalkyl;~~

Y (the  $\alpha$ -atom) is a CH group;

Cy is 2-trifluoromethylthiophenyl, 2-dimethylaminophenyl, 2-ethoxycarbonylmethoxyphenyl, an optionally  $R_{3a}$  substituted phenyl, naphthyl or cycloalkyl group, or a phenyl group substituted by  $R_{3i}X_i$  in which  $X_i$  is a bond, O, NH or  $CH_2$  and  $R_{3i}$  is phenyl, pyridyl or pyrimidinyl optionally substituted by  $R_{3a}$  is a saturated or unsaturated, mono or poly cyclic, homocyclic group, optionally substituted by groups  $R_{3a}$  or  $R_{3i}X_i$ ;

each  $R_{3a}$  independently is hydrogen; hydroxyl; alkoxy; aralkyloxy; carboxyalkoxy; alkyl; alkylaminoalkyl; hydroxymethyl; carboxy; alkoxyalkyl; alkoxyacetyl; alkylaminocarbonyl; aminomethyl;  $CONH_2$ ;  $CH_2CONH_2$ ; (1-6C)alkanoylamino; alkoxyacetylaminomethyl; amino; halo; cyano; nitro; thiol; alkylthio; alkylsulphonyl; alkylsulphenyl; alkylsulphonamido; alkylaminosulphonyl; aminosulphonyl; haloalkoxy; haloalkyl; a group of the formula  $-C(X^3)N(R^{11})R^{12}$  (wherein  $X^3$  is O or S and  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen, methyl, ethyl, or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group; or  $-OCH_2O-$  which is bonded to two adjacent ring atoms in CyR<sub>1a</sub>, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphenyl, alkylsulphonyl, triazolyl, imidazolyl, tetrazolyl, hydrazide, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkylloxazolyl,

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

.. 7 -

~~oxazolyl, alkylsulphonamido, alkylamino sulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula  $C(X^3)N(R^{11})R^{12}$  (wherein  $X^3$  is O or S, and  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group), or  $OCH_2O$  which is bonded to two adjacent ring atoms in Cy;~~

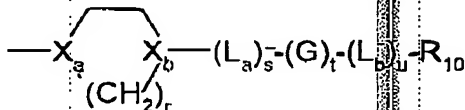
$X_1$  is a bond, O, NH or  $CH_2$ ;

$R_{3i}$  is phenyl, pyridyl or pyrimidinyl optionally substituted by  $R_{3a}$ ; and

~~$R_{1e}$  and  $R_{1j}$  are as defined for  $R_{1a}$~~

~~L is  $CONH$ ,  $CH_2NHCO$ ,  $CONHCH_2$ ,  $CONHCH_2CH_2$  or  $CON(Me)CH_2$  an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; and~~

$Lp(D)_n$  is of the formula:



in which:

$r$  is 1 or 2;

$X_a$  is CH and  $X_b$  is N;

$s$ ,  $t$  and  $u$  are each 0 or 1;

$L_a$  and  $L_b$  are each independently selected from a single bond, C=O, O and  $NR_{1e}$ , in which  $R_{1e}$  is hydrogen or (1-6C)alkyl;

G is (1-6C)alkanediyl; and

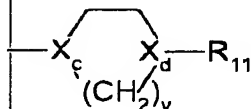
$R_{10}$  is (1-6C)alkyl; (3-6C)cycloalkyl [which is unsubstituted or substituted by (1-6C)alkyl]; indanyl; pyridyl; tetrahydropyranyl; tetrahydrothiopyranyl; phenyl {which is unsubstituted or substituted by one or two  $R_3$  groups [wherein  $R_3$  is hydrogen, hydroxyl, alkoxy, (1-6C)alkyl, (1-6C)alkylamino (1-6C)alkyl, (1-6C)alkanoyl alkyl (optionally

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 8 -

~~substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), (1-6C)hydroxyalkyl, carboxy, carboxy(1-5C)alkyl, hydroxyalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl, aminomethyl, aminocarbonyl, aminocarbonyl(1-5C)alkyl, aminoalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), methylamino, dimethylamino, ethylamino, formylamino, acetylaminomethyl, acetylaminomethyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, or haloalkyl}, pyrrolinyl; or a group of formula:~~



in which  $v$  is 1, 2 or 3; one of  $X_c$  and  $X_d$  is N and the other is CH or N (provided that when  $v$  is 1,  $X_c$  and  $X_d$  are not both N); and  $R_{11}$  is hydrogen, (1-6C)alkyl or when  $X_d$  is CH, hydroxy(1-6C)alkyl; provided that when  $t$  is 0, the sum of  $s$  and  $u$  is 1; when  $X_b$  is N,  $L_a$  is a bond or C=O; when  $X_c$  is N,  $L_b$  is a bond or C=O; when  $X_b$  and  $X_c$  are both N,  $t$  is 1; and when  $(L_a)_s$ -(G) $_t$ -(L $_b$ ) $_u$  represents an alkyl group and  $X_b$  and  $X_c$  both represent N, the alkyl group contains at least two chain carbon atoms;

or  $R_{10}$  is hydrogen and  $s$ ,  $t$  and  $u$  are each 0;

~~or the compound of formula (I) that is 4-([4-methoxybenzoyl D,L-(2-trifluoromethylthiophenyl)]~~

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 9 -

~~glycinyllaminomethyl]-1-isopropylpiperidine,~~

but excluding the compound 4-[(3-ethoxybenzoyl-D,L-phenylglycinyllaminomethyl]-1-[4-chlorobenzyl]piperidine;  
or a physiologically tolerable salt thereof.

2 (currently amended): A serine protease inhibitor according to claim 1,

wherein:

~~R<sub>2</sub> is a 5 or 6 membered aromatic carbon ring optionally interrupted by a nitrogen, oxygen or sulphur ring atom, optionally being substituted in the 3 and/or 4 position (in relation to the point of attachment of X-X) by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri- or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub>, or R<sub>1</sub>, or the substituents at the 3 or 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>, and optionally substituted in the position alpha to the X-X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxy, carbonyl, cyano, amide, aminoalkyl, alkoxy or alkylthio with the proviso that R<sub>2</sub> cannot be aminoisquinolyl,~~

~~— each X independently is a C, N, O or S atom or a CO, CR<sub>1a</sub>, C(R<sub>1a</sub>)<sub>2</sub> or NR<sub>1a</sub> group, at least one X being C, CO, CR<sub>1a</sub> or C(R<sub>1a</sub>)<sub>2</sub>,~~

~~— each R<sub>1a</sub> independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxy, carbonyl, alkylamino, carbonyl, alkoxy, carbonyl, amino, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl,~~

~~— R<sub>1</sub> is as defined for R<sub>1a</sub>, provided that R<sub>1</sub> is not~~



Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 10 -

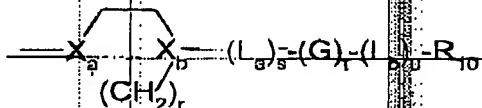
~~unsubstituted aminoalkyl,~~~~Y (the  $\alpha$  atom) is a CH group;~~

~~Cy is an optionally  $R_{3a}$  substituted: phenyl, naphthyl or cycloalkyl group is a saturated or unsaturated, mono or poly cyclic, homocyclic group optionally substituted by groups  $R_{3a}$  or phenyl optionally substituted by  $R_{3a}$ .~~

~~each  $R_{3a}$  independently is hydrogen; hydroxyl; alkoxy; alkyl; alkylaminoalkyl; hydroxymethyl; carboxy; alkoxyalkyl; alkoxycarbonyl; alkylaminocarbonyl; aminomethyl;  $\text{CONH}_2$ ;  $\text{CH}_2\text{CONH}_2$ ; (1-6C)alkanoylamino; alkoxycarbonylamino; amino; halo; cyano; nitro; thiol; alkylthio; alkylsulphonyl; alkylsulphenyl; alkylsulphonamido; alkylaminosulphonyl; aminosulphonyl; haloalkoxy or haloalkyl; ~~cyano, nitro, thiol, alkylthio, alkylsulphenyl, alkylsulphonyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy or haloalkyl and~~~~

 ~~$R_{1c}$  and  $R_{1j}$  are as defined for  $R_{1a}$~~ 

~~L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; and~~

 ~~$\text{Ip}(D)_n$  is of the formula:~~~~in which:~~~~r is 1 or 2;~~ ~~$X_a$  is CH and  $X_b$  is N;~~~~s, t and u are each 0 or 1;~~

Serial No. 10/030,188

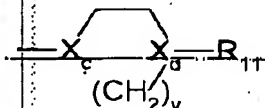
Reply to Office Action of Oct. 22, 2003

- 11 -

~~$L_a$  and  $L_b$  are each independently selected from a single bond, C-O, O and  $NR_{1e}$ , in which  $R_{1e}$  is hydrogen or (1-6C)alkyl,~~

~~G is (1-6C)alkanediyl; and~~

~~$R_{10}$  is (1-6C)alkyl, (3-6C)cycloalkyl [which is unsubstituted or substituted by (1-6C)alkyl], indanyl, pyridyl, tetrahydropyranyl, tetrahydrothiopyranyl, phenyl [which is unsubstituted or substituted by one or two  $R_3$  groups [wherein  $R_3$  is hydrogen, hydroxyl, alkoxy, alkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), hydroxyalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl, aminoalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkylamino (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), amine, halo, cyano, nitro, thiol, alkylthio, alkylsulphenyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkyl-oxazolyl, oxazolyl, alkylsulphenamide, alkylaminosulphenyl, aminesulphenyl, haloalkoxy or haloalkyl], pyrrolinyl, or a group of formula-~~



~~in which  $v$  is 1, 2 or 3, one of  $X_c$  and  $X_d$  is N and the other is CH or N, provided that when  $v$  is 1,  $X_c$  and  $X_d$  are not both N, and  $R_{11}$  is hydrogen, (1-6C)alkyl or when  $X_d$  is CH, hydroxy(1-6C)alkyl, provided that when  $v$  is 0, the sum of  $s$  and  $u$  is 1, when  $X_b$  is N,  $L_a$  is a bond or C-O, when  $X_c$  is N,~~

Serial No. 10/030,188

Reply to Office Action of Oct 22, 2003

- 12 -

~~$L_b$  is a bond or C-O, when  $X_b$  and  $X_e$  are both N,  $t$  is 1, and when  $(L_a)_s$  (O) $_t$   $(L_b)_u$  represents and alkyl group and  $X_b$  and  $X_e$  both represent N, the alkyl group contains at least two chain carbon atoms,~~

~~or a physiologically tolerable salt thereof.~~

3 (previously presented): A serine protease inhibitor according to claim 1, wherein  $R^3$  is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, propyl, 2-propyl, butyl, 2-butyl, t-butyl, pentyl, 2-pentyl, 3-pentyl, isopropylaminomethyl, dimethylamino-methyl, diethylaminomethyl, dimethylaminoethyl, acetyl, hydroxymethyl, hydroxyethyl, carboxy, carboxy(1-5C)alkyl, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminomethyl, aminocarbonyl, aminocarbonyl(1-5C)alkyl, methylamino, dimethylamino, ethylamino, formylamino, acetylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, isopropylsulphonyl, methylsulphenyl, 1,2,4-triazol-2-yl, 1,2,4-triazol-4-yl, 1,2,3-triazol-4-yl, 1,3-imidazol-1-yl, 1,3-imidazol-4-yl, tetrazol-1-yl, tetrazol-5-yl, methylsulphonamido, ethylsulphonamido, propylsulphonamido, methylaminosulphonyl, ethylaminosulphonyl, propylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl and trichloromethyl.

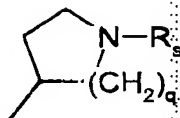
4 (previously presented): A compound according to claim 1 wherein  $r$  is 2.

5 (original): A compound according to claim 1 wherein  $L_p(D)_n$  is of the formula:

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 13 -



wherein:

q is 1 or 2;

$R_s$  is hydrogen,  $-(CH_2)_c-R_c$ ,  $-CHR_eR_f$ , or  $-CH_2-CHR_eR_f$  [c is 0, 1 or 2; wherein  $R_c$  is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl,  $CONH_2$ ,  $SO_2NH_2$ , methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and  $R_e$  and  $R_f$  are independently hydrogen or  $C_{1-3}$ alkyl; or  $CHR_eR_f$  is (3-6C)cycloalkyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position, provided the substituent is not bonded to the CH group which is bonded to L), tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl (which may bear a 1-methyl substituent), piperidinyl (which may bear a 1-methyl substituent) (provided that the tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl and piperidinyl rings are not linked to the piperidin-1,4-diyl group through a ring nitrogen atom or a ring carbon atom adjacent to a ring oxygen, sulfur or nitrogen atom) or indan-2-yl].

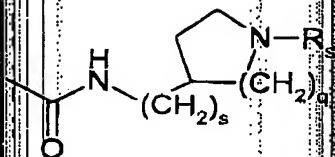
6 (canceled).

7 (original) A serine protease inhibitor according to claim 2 wherein  $-L-Lp(D)_n$  is of the formula:

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 14 -



wherein

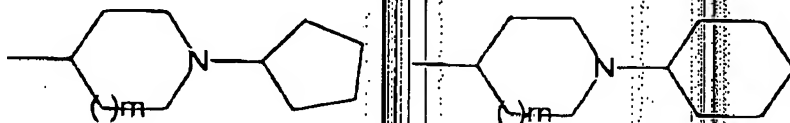
q is 1 or 2;

s is 0 or 1; and

$R_5$  is  $-(CH_2)_c-R_C$ ,  $-CH(R_e)R_f$ , or  $-CH_2-CH(R_e)R_f$  [wherein c is 1 or 2;  $R_C$  is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl,  $CONH_2$ ,  $SO_2NH_2$ , methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and  $R_e$  and  $R_f$  are independently hydrogen or  $C_{1-3}$ alkyl; or  $CH(R_e)R_f$  is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), piperidin-4-yl (which may bear a 1-methyl substituent), or indan-2-yl].

8 (previously presented): A compound according to claim 5 wherein q is 2.

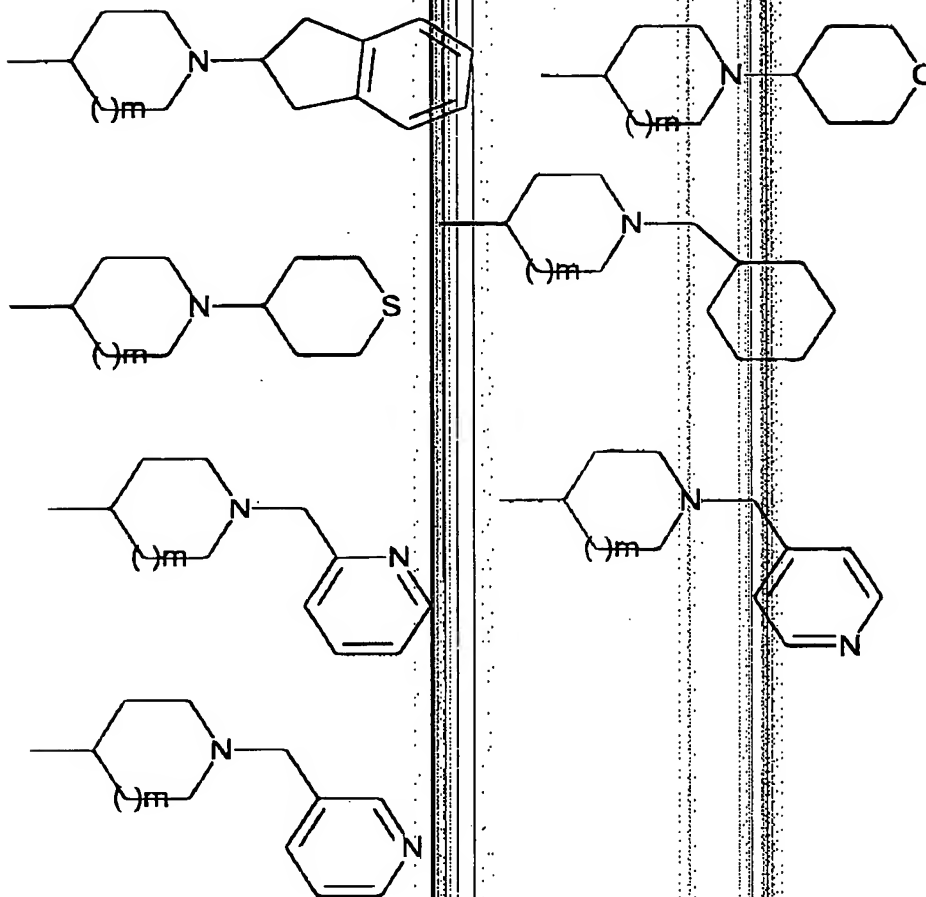
9 (previously presented): A compound according to claim 1 wherein  $Lp(D)_n$  is selected from one of the following formulae:



Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 15 -



wherein m represents 0 or 1.

10 (previously presented): A compound according to claim 7 wherein  $R_8$  is selected from: hydrogen, methyl, ethyl, prop-2-yl, but-2-yl, pent-3-yl, hept-4-yl, cyclopentyl, cyclohexyl, cyclohexylmethyl, 1-methylpiperidin-4-yl, tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, phenyl, benzyl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, pyrid-3-ylmethyl, pyrid-4-ylmethyl and indan-2-yl.

11 (canceled).

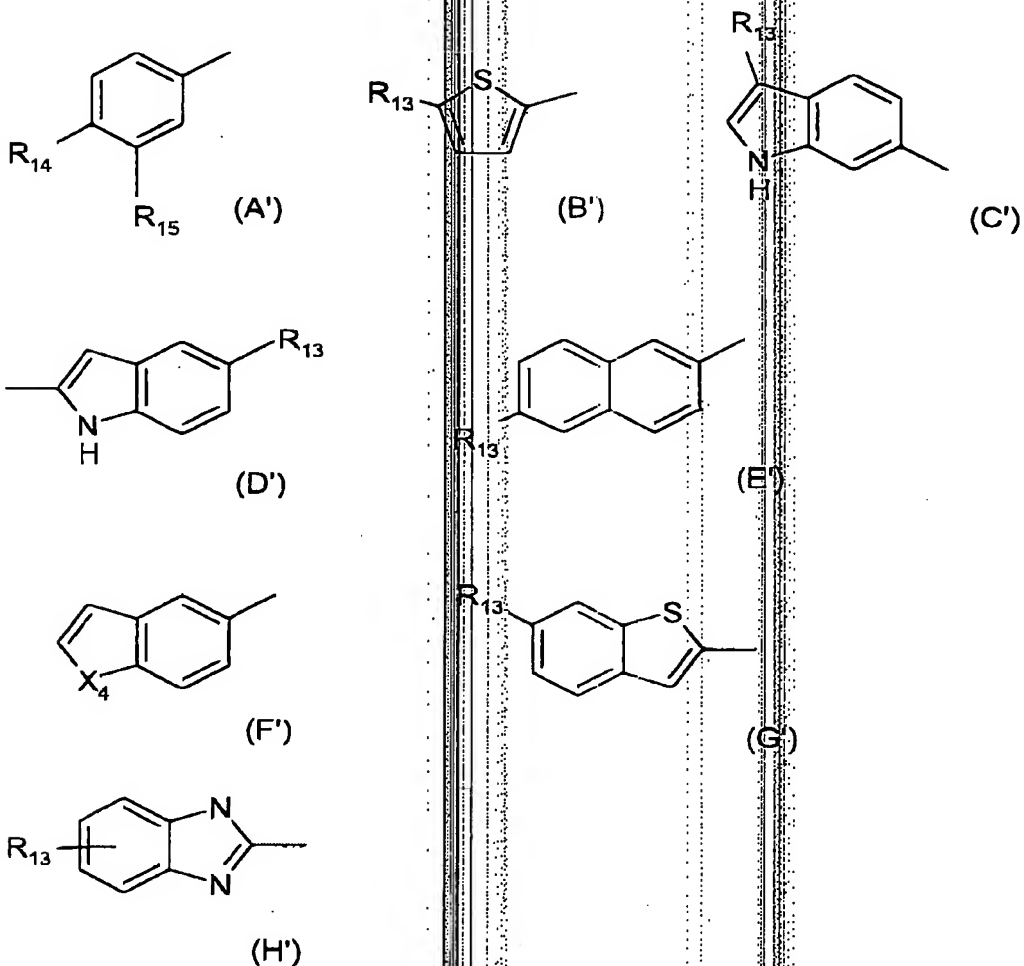
Serial No. 10/030,188

Reply to Office Action of Oct 22, 2003

- 16 -

12 (canceled).

13 (previously presented) A compound according to claim 1 wherein  $R_2$  is selected from one of the formula (A') to (H'):



wherein  $X_4$  is O or S,  $R_{13}$  is selected from hydrogen, fluoro, chloro or methyl and  $R_{14}$  is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and  $R_{15}$  is selected from hydrogen, methyl, fluoro, chloro and amino.

14 (previously presented) A compound according to claim 1,

Serial No. 10/030,188

Reply to Office Action of Oct 22, 2003

- 1.7 -

wherein  $R_2$  is 4-methoxyphenyl, 3-amino-4-chlorophenyl, indol-2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl.

15 (canceled).

16 (canceled).

17 (canceled):

18 (canceled):

19 (canceled)

20 (canceled)

21 (previously presented): A compound according to claim 1 wherein  $R_{3a}$  is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl,  $\text{CONH}_2$ ,  $\text{CH}_2\text{CONH}_2$ , acetylamino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, bromo, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl, pyrrolidin-1-ylcarbonyl, piperidin-1-ylcarbonyl, morpholin-1-ylcarbonyl and  $-\text{OCH}_2\text{O}-$  (which is bonded to two adjacent ring atoms in Cy).

22 (previously presented): A compound according to claim 1 wherein  $R_{3a}$  is selected from hydrogen, hydroxyl, methoxy,



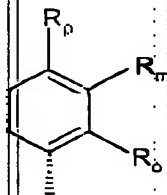
Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 18 -

ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl,  $\text{CONH}_2$ ,  $\text{CH}_2\text{CONH}_2$ , acetyl amino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy and trifluoromethyl.

23 (previously presented): A compound according to claim 1 wherein Cy is



wherein:

$R_o$  is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphenyl and methylsulphonyl;

$R_m$  is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphenyl, methylsulphonyl, carboxy, methoxycarbonyl and a group of the formula  $-\text{C}(\text{X}^3)\text{N}(\text{R}^{11})\text{R}^{12}$  (wherein  $\text{X}^3$  is O or S and  $\text{R}^{11}$  and  $\text{R}^{12}$  are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group);  $R_p$  is selected from hydrogen and fluoro; or

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 19 -

$R_O$  and  $R_m$  or  $R_m$  and  $R_D$  form an  $-OCH_2O-$  group; or  
 $R_O$  and  $R_m$  together with the ring to which they are attached  
form a 6 membered aryl ring.

24 (previously presented): A compound according to claim 1  
wherein Cy is selected from phenyl, 2-chlorophenyl, 2-  
methoxyphenyl, 4-carbamoylphenyl and naphthyl.

25 (currently amended): A compound as claimed in any one of  
claims ~~1-15, 17-18 and 21-24~~ 1-5, 7-10, 13-14 and 21-24, in  
which the alpha atom in Y has the conformation that would  
result from construction from a D- $\alpha$ -aminoacid  $NH_2-CH(Cy)-COOH$   
where the  $NH_2$  represents part of X-X

26 (previously presented): A pharmaceutical composition, which  
comprises a compound as claimed in claim 1 together with at  
least one pharmaceutically acceptable carrier or excipient.

27 (canceled).

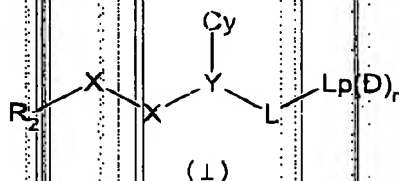
28 (canceled).

29 (currently amended): A method of treatment of a human or  
non-human animal body to combat a thrombotic disorder selected  
from venous thrombosis, pulmonary embolism, arterial  
thrombosis, myocardial ischaemia, myocardial infarction and  
cerebral thrombosis, which comprises administering to said  
body an effective amount of a serine protease inhibitor of  
formula (I):

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 20 -



wherein:

R<sub>2</sub> is:

(i) phenyl optionally being substituted in the 3 and/or 4 position by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub>- or R<sub>1</sub>, and optionally substituted at the 6 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(ii) naphth-2-yl optionally substituted at the 6 or 7 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>; and optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(iii) isoquinolin-1-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 21 -

(viii) pyrazol-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(ix) pyrid-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(x) pyrid-3-yl optionally substituted at the 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(xi) benzofur-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(xii) indol-2-yl optionally substituted on the indole nitrogen atom by alkyl and optionally substituted at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(xiii) indol-6-yl substituted at the 5 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio and optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>; or

(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

R<sub>1</sub> is hydrogen; hydroxy; alkoxy; alkyl; alkylaminoalkyl; alkanoyl; hydroxyalkyl; alkoxyalkyl; alkoxycarbonyl; alkylaminocarbonyl; alkylamino; carboxyl; carboxymethyl; amido (CONH<sub>2</sub>) or amidomethyl;

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

22 -

R<sub>1j</sub> is: hydrogen; hydroxy; alkoxy; alkyl; alkanoyl; hydroxyalkyl; alkoxyalkyl; alkoxycarbonyl; alkylamino; carboxyl; carboxymethyl; amido (CONH<sub>2</sub>) or amidomethyl; a 5 or 6 membered aromatic carbon ring optionally interrupted by a nitrogen, oxygen or sulphur ring atom, optionally being substituted in the 3 and/or 4 position (in relation to the point of attachment of X-X) by halo, nitro, thiol, haloalkoxy, hydrazide, alkylhydrazide, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub> or R<sub>1</sub>, or the substituents at the 3 or 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazide, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>, and optionally substituted in the position alpha to the X-X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio with the proviso that R<sub>2</sub> cannot be aminoisoquinolyl;

X-X is CONH;

each X independently is a C, N, O or S atom or a CO, CR<sub>1a</sub>, C(R<sub>1a</sub>)<sub>2</sub> or NR<sub>1a</sub> group, at least one X being C, CO, CR<sub>1a</sub> or C(R<sub>1a</sub>)<sub>2</sub>

each R<sub>1a</sub> independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;

R<sub>1</sub> is as defined for R<sub>1a</sub>, provided that R<sub>1</sub> is not unsubstituted aminoalkyl;

Y (the α-atom) is a CH group;

Cy is 2-trifluoromethylthiophenyl, 2-dimethylaminophenyl, 2-ethoxycarbonylmethoxyphenyl, an optionally R<sub>3a</sub> substituted:

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 23 -

phenyl, naphthyl or cycloalkyl group, or a phenyl group substituted by  $R_{3i}X_i$  in which  $X_i$  is a bond, O, NH or  $CH_2$  and  $R_{3i}$  is phenyl, pyridyl or pyrimidinyl optionally substituted by  $R_{3a}$  is a saturated or unsaturated, mono or poly cyclic, homocyclic group, optionally substituted by groups  $R_{3a}$  or  $R_{3i}X_i$ ;

each  $R_{3a}$  independently is hydrogen; hydroxyl; alkoxy; aralkyloxy; carboxyalkoxy; alkyl; alkylaminoalkyl; hydroxymethyl; carboxy; alkoxyalkyl; alkoxycarbonyl; alkylaminocarbonyl; aminomethyl;  $CONH_2$ ;  $CH_2CONH_2$ ; (1-6C)alkanoylamino; alkoxycarbonylamino; amino; halo; cyano; nitro; thiol; alkylthio; alkylsulphonyl; alkylsulphenyl; alkylsulphonamido; alkylaminosulphonyl; aminosulphonyl; haloalkoxy; haloalkyl; a group of the formula  $-C(X^3)N(R^{11})R^{12}$  (wherein  $X^3$  is O or S and  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen, methyl, ethyl, or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group; or  $-OCH_2O-$  which is bonded to two adjacent ring atoms in  $CyR_{1e}$ , amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphenyl, alkylsulphonyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkylloxazolyl, oxazolyl, alkylsulphenamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula  $-C(X^3)N(R^{11})R^{12}$  (wherein  $X^3$  is O or S, and  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group), or  $OCH_2O$  which is bonded to two adjacent ring atoms in  $Cy$ ;

$X_i$  is a bond, O, NH or  $CH_2$ ;

$R_{3i}$  is phenyl, pyridyl or pyrimidinyl optionally substituted by  $R_{3a}$ ; and

$R_{1e}$  and  $R_{1j}$  are as defined for  $R_{1a}$ .

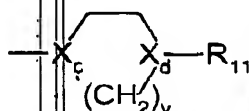


Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 25 -

cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, or haloalkyl}}, pyrrolinyl; or a group of formula:



in which  $v$  is 1, 2 or 3; one of  $X_c$  and  $X_d$  is N and the other is CH or N (provided that when  $v$  is 1,  $X_c$  and  $X_d$  are not both N); and  $R_{11}$  is hydrogen, (1-6C)alkyl or when  $X_d$  is CH, hydroxy(1-6C)alkyl; provided that when  $t$  is 0, the sum of  $s$  and  $u$  is 1; when  $X_b$  is N,  $L_a$  is a bond or C=O; when  $X_c$  is N,  $L_b$  is a bond or C=O; when  $X_b$  and  $X_c$  are both N,  $t$  is 1; and when  $(L_a)_s - (G)_t - (L_b)_u$  represents an alkyl group and  $X_b$  and  $X_c$  both represent N, the alkyl group contains at least two chain carbon atoms;

or  $R_{10}$  is hydrogen and  $s$ ,  $t$  and  $u$  are each 0;

~~or the compound of formula (I) that is 4-{[4-methoxybenzoyl D,L (2-trifluoromethylthiophenyl)-glycinyl]aminomethyl} 1-isopropylpiperidine,~~  
or a physiologically-tolerable salt thereof.

30 (canceled).

31 (canceled).

32 (currently amended) A compound according to Claim 1 wherein:

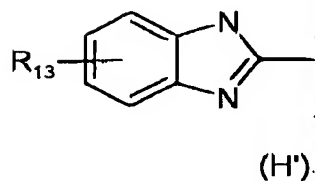
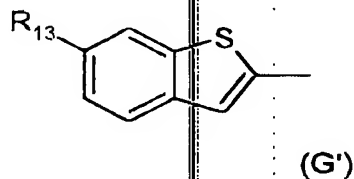
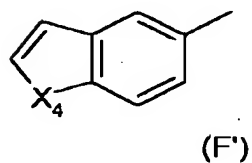
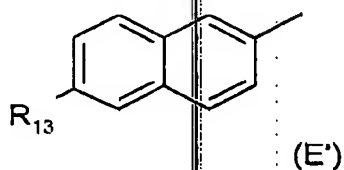
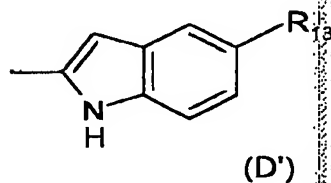
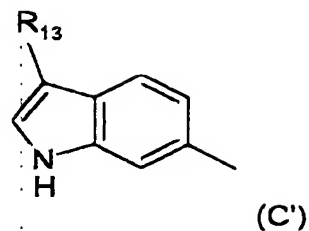
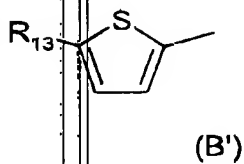
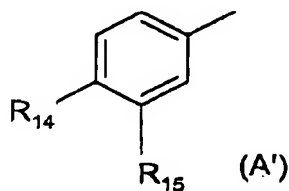
$R_2$  is selected from one of the formula (A') to (H'):



Serial No. 10/030.188

Reply to Office Action of Oct. 22, 2003

25



wherein  $X_4$  is O or S,  $R_{13}$  is selected from hydrogen, fluoro, chloro or methyl and  $R_{14}$  is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and  $R_{15}$  is selected from hydrogen, methyl, fluoro, chloro and amino;

~~X-X represents CONH-~~

Y (the  $\alpha$ -atom) is ~~CH~~ and has the conformation that would result from construction from a D- $\alpha$ -aminoacid

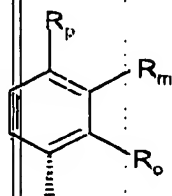
$NH_2-CH(Cy)-COOH$  where the  $NH_2$  represents part of X-X;

Cy is

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

27



wherein:

$R_o$  is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl and methylsulphonyl;

$R_m$  is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl, methylsulphonyl, carboxy, methoxycarbonyl and a group of the formula  $-C(X^3)N(R^{11})R^{12}$  (wherein  $X^3$  is O or S and  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group); and

$R_p$  is selected from hydrogen and fluoro; or

$R_o$  and  $R_m$  or  $R_m$  and  $R_p$  form an  $-OCH_2O-$  group; or

$R_o$  and  $R_m$  together with the ring to which they are attached form a 6 membered aryl ring;

and

$L$  is  $CONH$ ,  $CH_2NHCO$ ,  $CONHCH_2$ ,  $CONHCH_2CH_2$  or  $CON(Me)CH_2$ .

33 (previously presented): A compound according to Claim 32 wherein

$R_2$  is 4-methoxyphenyl, 3-amino-4-chlorophenyl, indol-2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl;

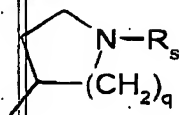
$Cy$  is selected from phenyl, 2-chlorophenyl, 2-methoxyphenyl, 4-carbamoylphenyl and naphthyl; and

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

28

$Lp(D)_n$  is of the formula:



wherein:

$q$  is 1 or 2;

$R_s$  is hydrogen,  $-(CH_2)_c-R_c$ ,  $-CHR_eR_f$ , or  $-CH_2-CHR_eR_f$  [ $c$  is 0, 1 or 2; wherein  $R_c$  is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl,  $CONH_2$ ,  $SO_2NH_2$ , methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and  $R_e$  and  $R_f$  are independently hydrogen or  $C_{1-3}$ alkyl; or  $CHR_eR_f$  is (3-6C)cycloalkyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position, provided the substituent is not bonded to the  $CH$  group which is bonded to  $L$ ), tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl (which may bear a 1-methyl substituent), piperidinyl (which may bear a 1-methyl substituent) (provided that the tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl and piperidinyl rings are not linked to the piperidin-1,4-diyl group through a ring nitrogen atom or a ring carbon atom adjacent to a ring oxygen, sulfur or nitrogen atom) or indan-2-yl].

34 (currently amended) - A compound according to Claim 2 wherein

$R_2$  represents:

(i) phenyl optionally being substituted in the 3 and/or 4 position by fluoro, chloro, bromo, iodo, nitro, difluoromethoxy, trifluoromethoxy, amino, cyano, trifluoromethyl, methylthio, vinyl, carboxy, acetoxy,  $MeSO_2-$ ,

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 29 -

hydroxy, methoxy, ethoxy, methyl, methoxycarbonyl, methylamino, ethylamino or amido, and optionally substituted at the 6 position by amino, hydroxy, fluoro, methoxycarbonyl, cyano or aminomethyl;

(ii) naphth-2-yl optionally substituted at the 6, position by hydroxy and optionally substituted at the 3 position by amino or hydroxy;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by chloro, bromo, amino, methyl or methoxy;

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by methylthio, methyl or acetyl;

(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) pyrazol-2-yl substituted at the 5 position by methyl;

(ix) pyrid-2-yl optionally substituted at the 6 position by chloro;

(x) pyrid-3-yl optionally substituted at the 4 position by chloro;

(xi) benzofur-2-yl optionally substituted at the 3 position by chloro, methyl or methoxy, at the 5 or 6 position by methyl and at the 6 position by methoxy;

(xii) indol-2-yl optionally substituted on the indole nitrogen atom by methyl and optionally substituted at the 5 or 6 position by fluoro, chloro, bromo, methyl or methoxy;

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

- 30 -

(xiii) indol-6-yl substituted at the 5 position by chloro, fluoro or hydroxy and optionally substituted at the 3 position by chloro or methyl; or

(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by fluoro, chloro or methyl, and optionally substituted at the 5 or 6 position by fluoro, chloro, methyl, hydroxy, or methoxy;

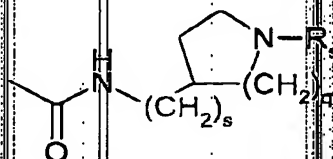
~~X-X represents CONH<sub>2</sub>~~

Y (the  $\alpha$ -atom) is CH and has the conformation that would result from construction from a D- $\alpha$ -aminoacid NH<sub>2</sub>-CH(Cy)-COOH where the NH<sub>2</sub> represents part of X-X;

~~Cy is an optionally R<sub>3a</sub> substituted phenyl, naphthyl or cycloalkyl group;~~

R<sub>3a</sub> is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, CONH<sub>2</sub>, CH<sub>2</sub>CONH<sub>2</sub>, acetyl amino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy and trifluoromethyl; and

-L-Lp(D)<sub>n</sub> is of the formula:



wherein

Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

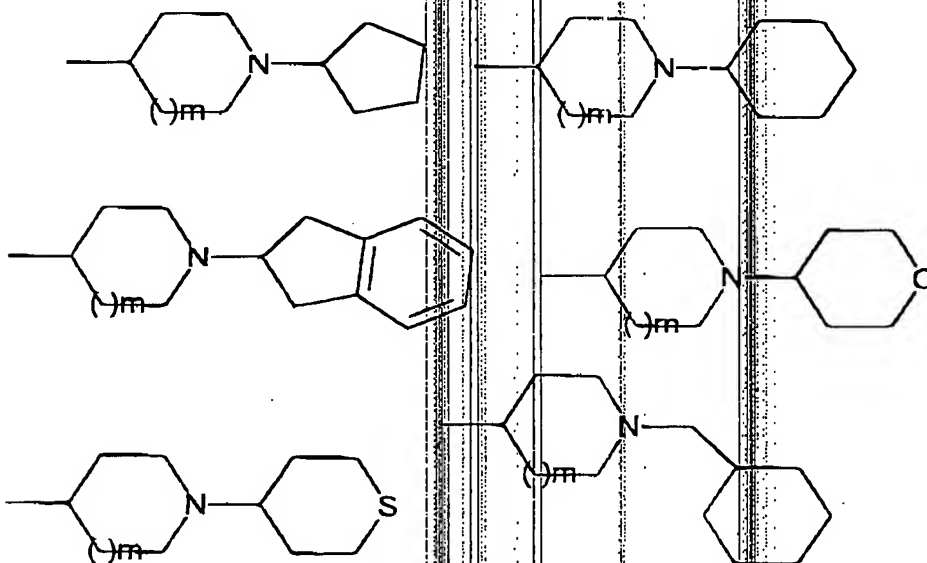
- 31 -

q is 1 or 2;

s is 0 or 1; and

$R_s$  is  $-(CH_2)_c-R_c$ ,  $-CHReR_f$ , or  $-CH_2-CHReR_f$  [wherein c is 1 or 2;  $R_c$  is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl,  $CONH_2$ ,  $SO_2NE_2$ , methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and  $R_e$  and  $R_f$  are independently hydrogen or  $C_{1-3}$ alkyl; or  $CHReR_f$  is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), piperidin-4-yl (which may bear a 1-methyl substituent), or indan-2-yl].

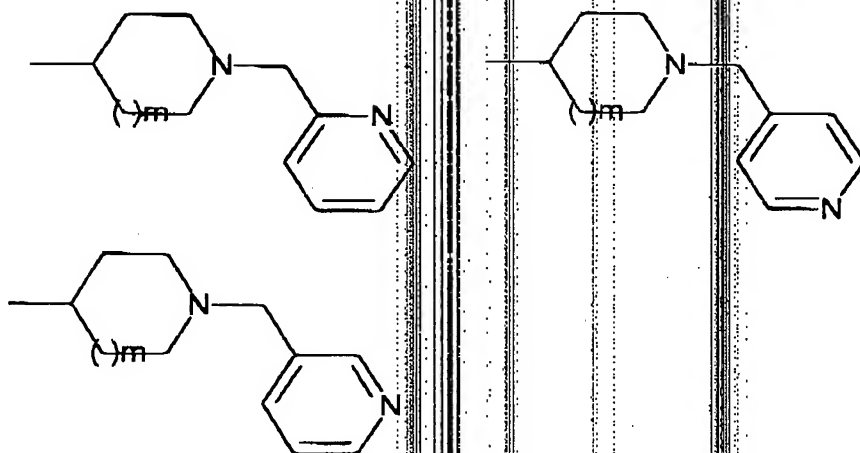
35 (previously presented). A compound according to Claim 34 wherein  $Lp(D)_n$  is selected from one of the following formulae:



Serial No. 10/030,188

Reply to Office Action of Oct. 22, 2003

32



wherein m represents 0 or 1.

36 (canceled):

37 (new): A compound as claimed in Claim 1, in which Cy is selected from phenyl, 2-fluorophenyl, 2-chlorophenyl, 2-bromophenyl, 2-iodophenyl, 2-methylphenyl, 2-methoxyphenyl, 2-ethoxyphenyl, 2-methylthiophenyl, 2-methylsulfonylphenyl, 2-t-butylthiophenyl, 2-t-butylsulfonylphenyl, 4-carbamoylphenyl, 2-trifluoromethylphenyl, 2-trifluoromethoxyphenyl, 2-trifluoromethylthiophenyl, 2-phenoxyphenyl, 2-benzyloxyphenyl, 2-nitrophenyl, 2-aminophenyl, 2-acetylamino-phenyl, 2-dimethylaminophenyl, 2-hydroxyphenyl, 2-ethoxycarbonyl-methoxyphenyl, 2-carboxymethoxyphenyl and cyclohexyl.